

Decline in Risk of HAV in China, a Country with Booming Economy & Changing Life Style

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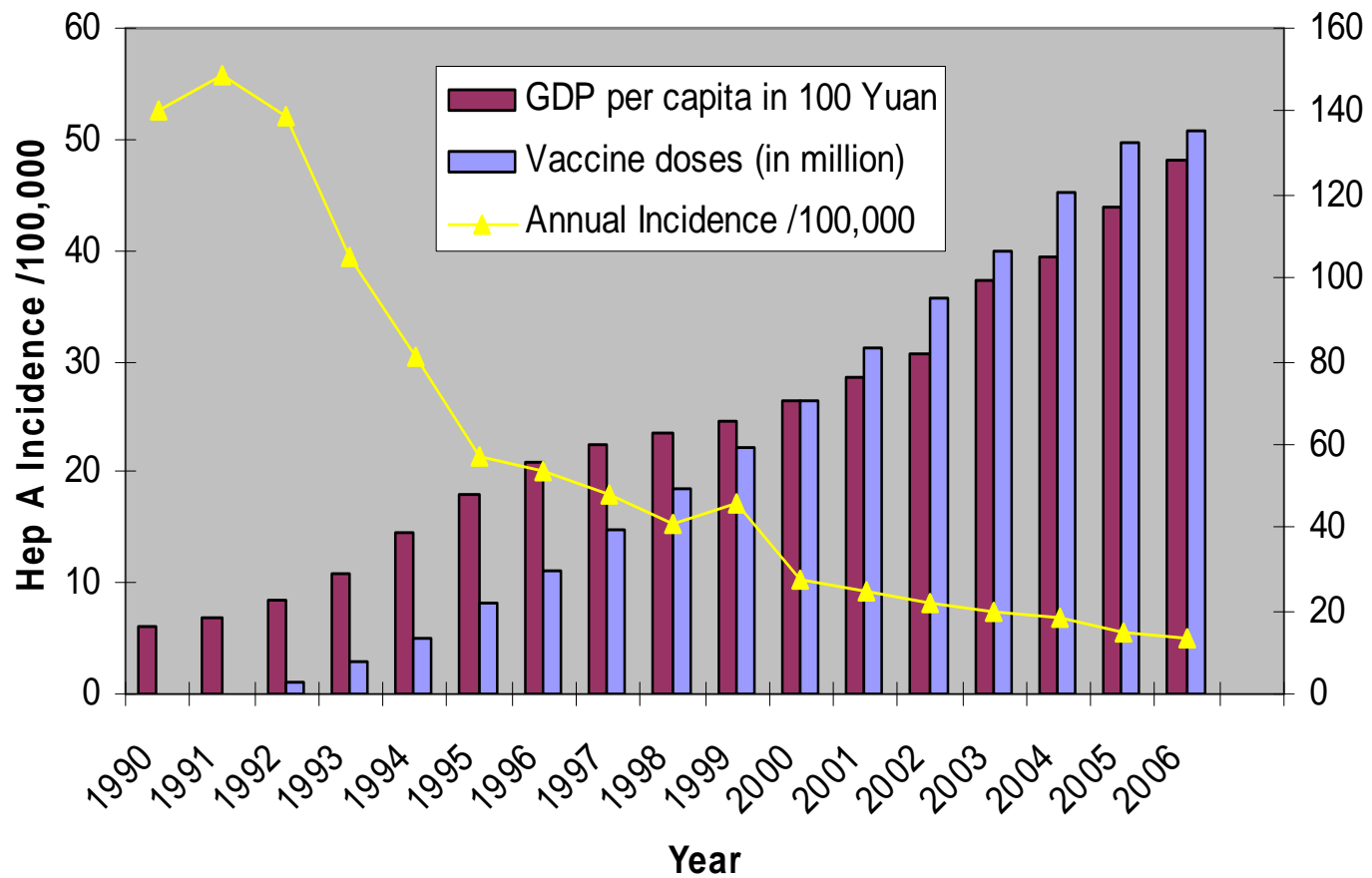
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Background

- The annual incidence rate of hepatitis A was reported as $>50/100,000$ in 1990-1992, & declined to $5/100,000$ in 2005-2006.
- The cumulative output of hepatitis A vaccine from a major manufacturer increased from 2.9 million doses in 1992 to 135.5 million doses in 2006.
- The GDP per capita increased from 1,622 Yuan (US\$200) in 1990 to 12,862 Yuan (US\$1,600) in 2006.

HAV Vaccine output, GDP and incidence in China 1990-2006



Causes for the Decline in HA Incidence in China

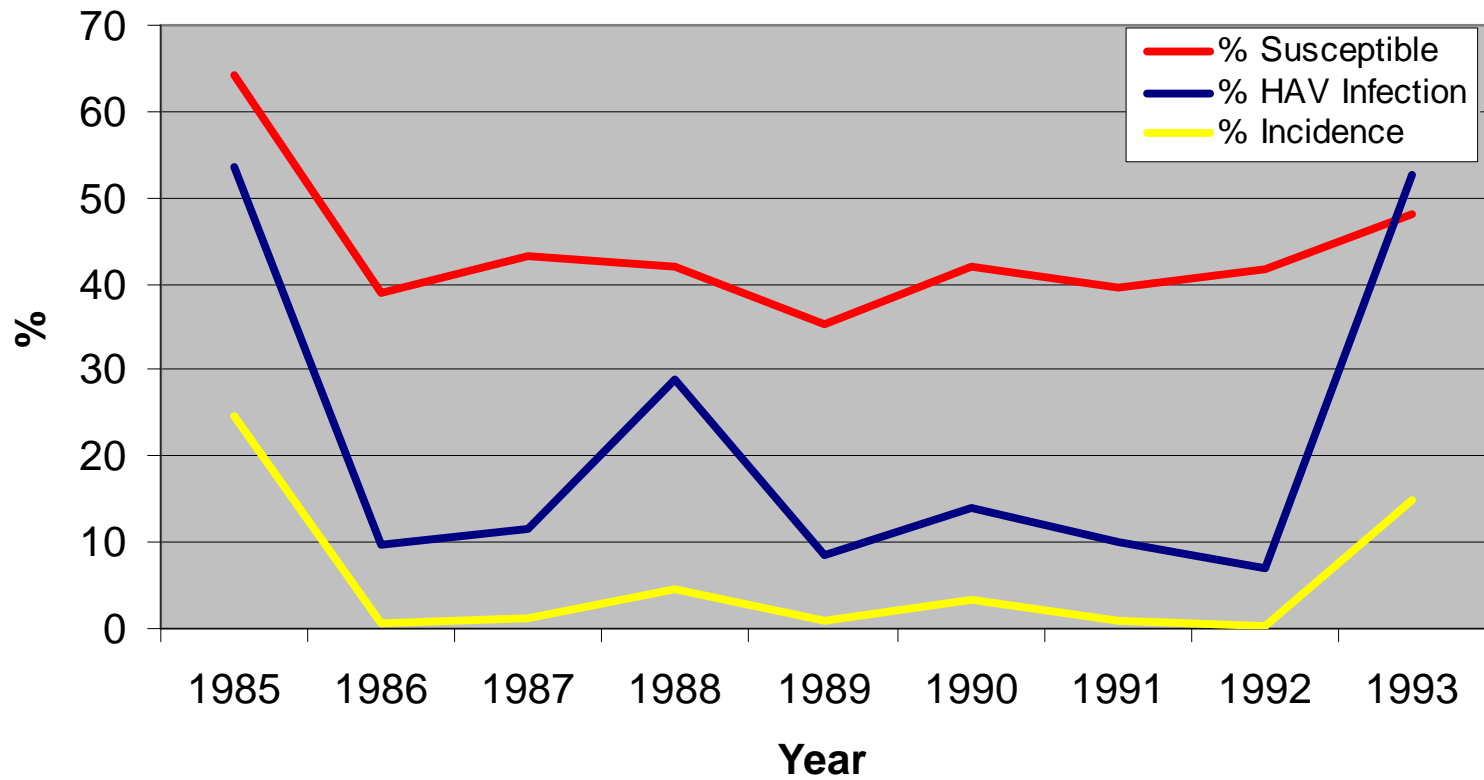
- Was the 90% decline in HAV risk attributable to HAV vaccine?
- Was the decline caused by changing life style associated with higher GDP & higher income?
- Both contributed to the decline?

Hepatitis A in Rural Hebei, a province in the North of China

HAV Epidemiology in Rural Hebei in pre- vaccination era

- In vast rural region, HA was characterized by cyclic epidemic and higher risk for children.
- Most people got infected by the age of 10.
- Poor hygiene, lack of safe water and watering toilet were the major risk factors.
- Risk and attack rate of HA varied with the change in proportion of susceptible individuals.
- An 8- year epidemic cycle with an average annualized risk of 0.20 was observed.

Annual Rates of HAV Infection, clinical disease and proportion of susceptible children < 15 years in Rural Hebei, China



Annualized HAV risk in kids <15 yrs. pre- (1986-93) & post- (96- 2004) vaccination eras, rural Hebei

| Year | HAV Vaccine | No. of Susceptible (person/year) | No. of New infections (person/year) | % |
|-----------|-------------|----------------------------------|-------------------------------------|------|
| 1986-1993 | No | 684 | 131 | 19.2 |
| 1996-2004 | No | 2,016 | 41 | 2.0 |
| | Yes | 2,192 | 8 | 0.6 |

Risk reduction post- vs. pre- vaccination: 93.94%

Risk reduction in unvaccinated post- vs. pre- vaccination: 89.92%

Risk reduction in vaccinated vs. unvaccinated post- vaccination: 82.27%

Causes for the HAV risk reduction

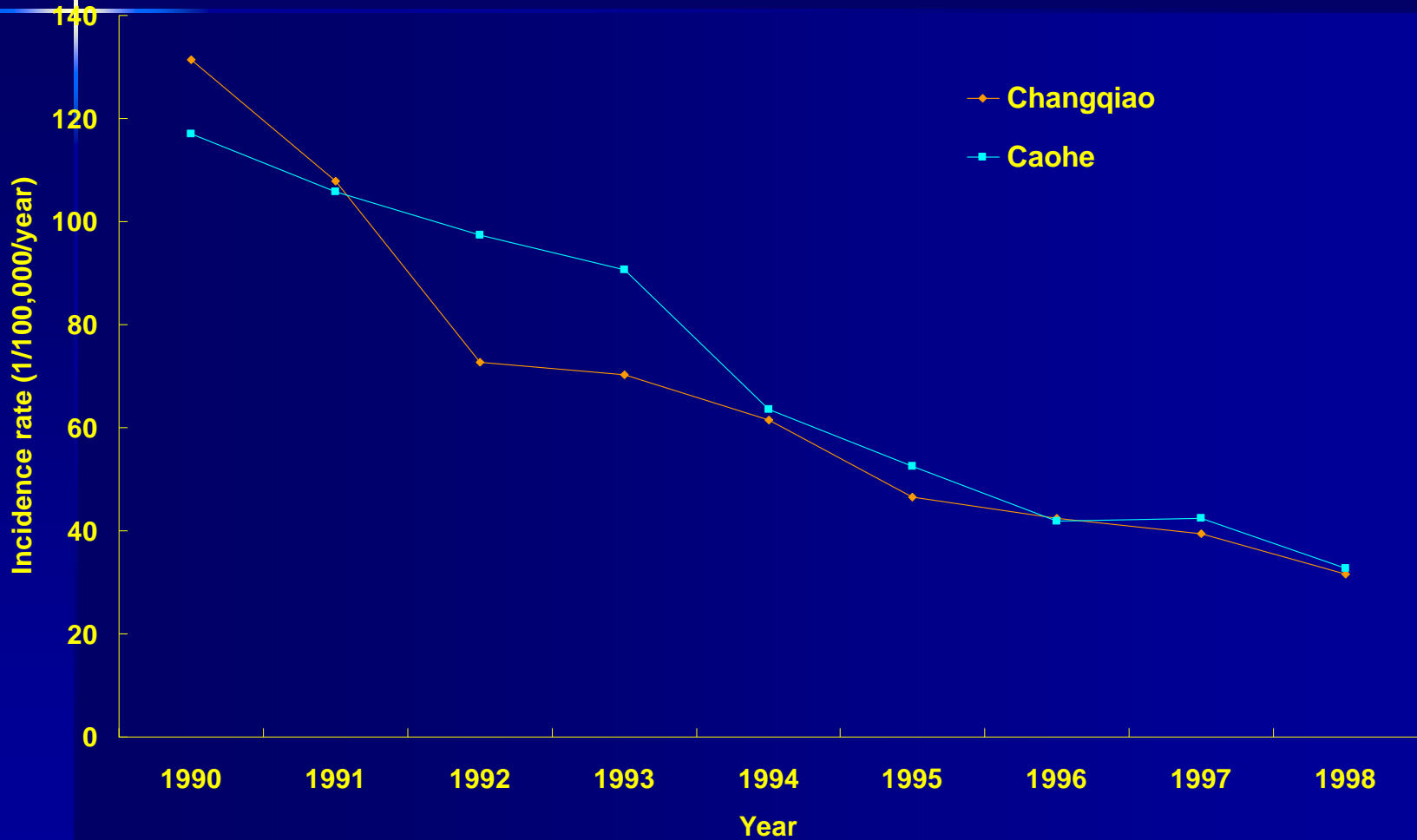
- Risk in vaccinated was lower than in unvaccinated by 82.3% during post- vaccination years.
- Vaccine efficacy against HAV infection was 82.3%
- Risk in unvaccinated children post- vs pre- vaccination years was reduced by 89.9%
- The higher risk reduction in unvaccinated children post- vs pre- vaccination (89.9%) than in the vaccinated vs unvaccinated (83.2%) can be explained more by changed life style than by indirect vaccine effectiveness.
- Both improved living conditions and vaccination led to the decline in risk of HAV in rural Hebei.

Hepatitis A in Shanghai, a Large City in the South of China

Decline in HAV risk in Shanghai, a well developed area

- HAV vaccine was introduced in Shanghai in 1994; a part of school children and university students received the vaccine at user's fee.
- HAV incidence rate declined in unvaccinated adults & unvaccinated children before HAV vaccine introduction in 1994

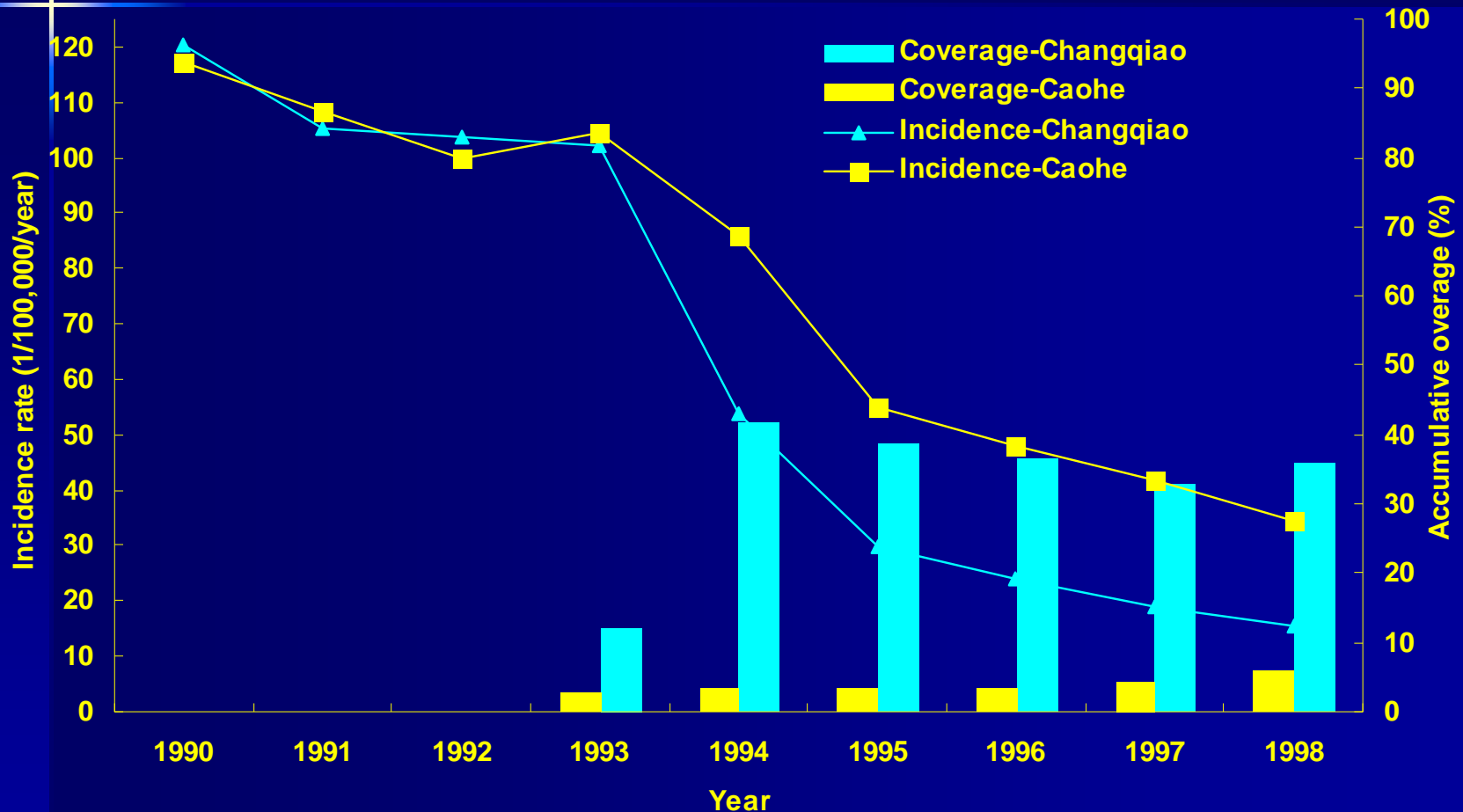
Annual HAV incidence rate in adults >25 yrs. unimmunized with HA vaccine in Changqiao and Caohe Districts, Shanghai, 1990 - 1998



Decline in HAV risk in subjects < 25 yrs, Changqiao and Caohe Districts

- Annual HAV incidence declined at the same pace before vaccine introduction in 1994.
- It declined more in Caohe with 50% vaccine coverage in students than in Changqiao with the coverage of 5%.
- The changed life style possibly accounted for 70% risk reduction, vaccine may contributed 30%.

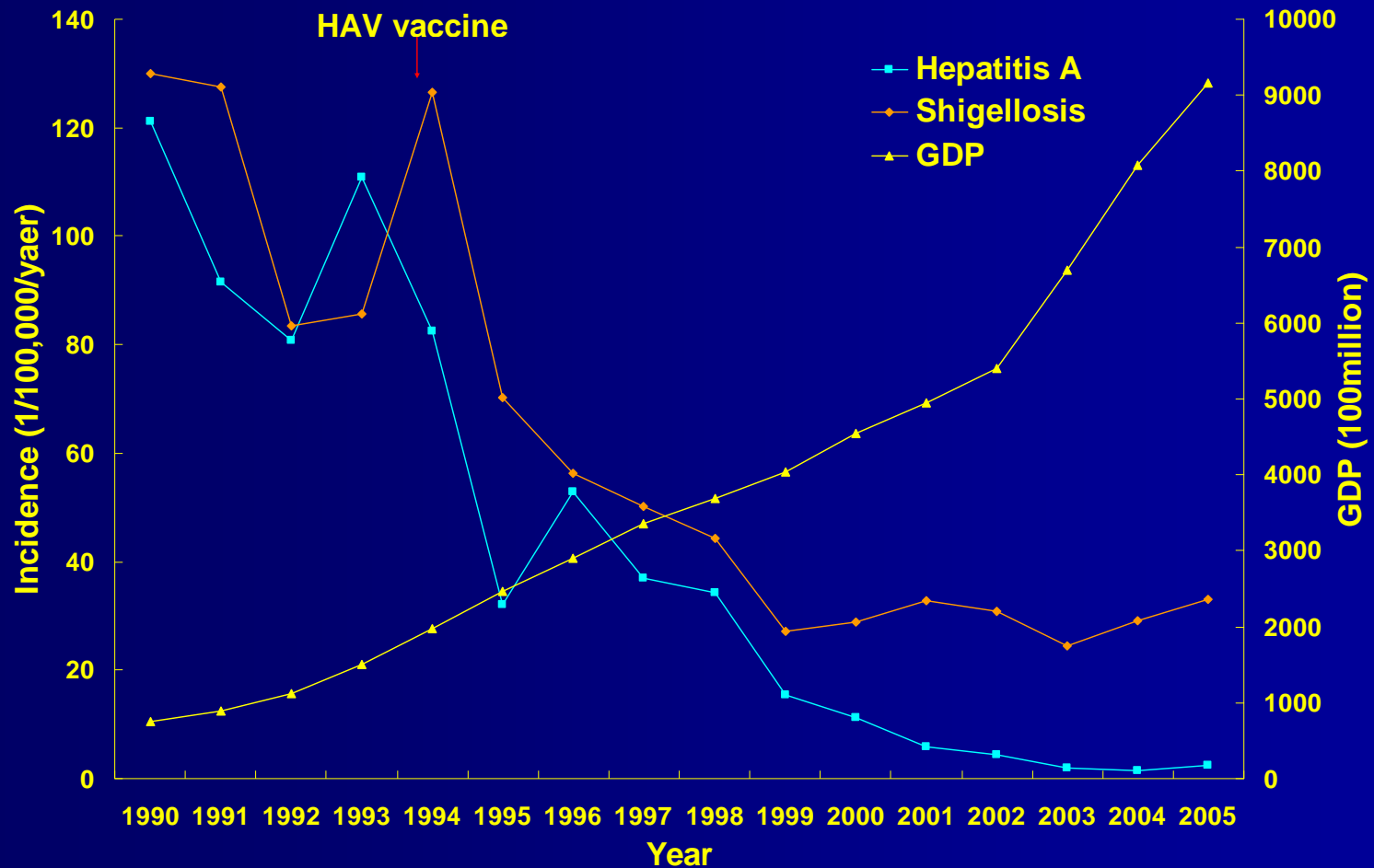
Decline in HAV risk in subjects < 25 yrs, Changqiao and Caohe Districts



Decline in rates of HAV & Shigelloses with increase in GDP, Shanghai, 1990-2005

- HAV and shigellosis declined at the same pace with the increase in GDP, Shanghai, 1990-1999.
- More rapid risk reduction for HAV was found only after 2000 when vaccinated children and sub-adults grew up.

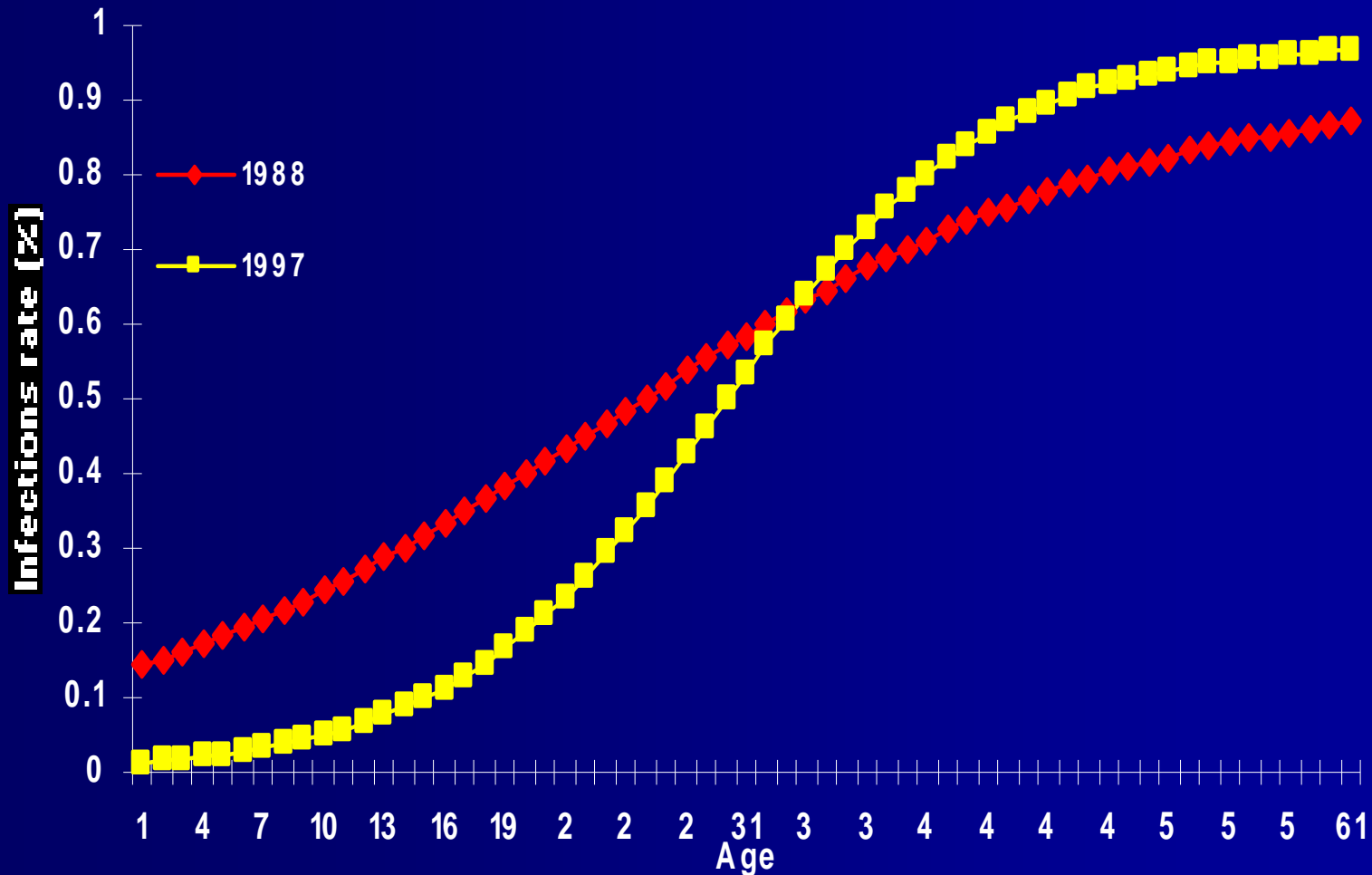
Decline in HAV & Shigelloses Rates with increase in GDP, Shanghai, 1990-2005



Should the decline in HA incidence rate be attributed to vaccination?

- From 1990 to 2005, annual shigellosis & HAV incidences dropped by 76% & 96% respectively. Vaccine was available for HA, not for shigellosis.
- Most residents moved to new flats with bigger living space and watering toilets during the last 30 years.
- Changed life style contributed more than the vaccination to the risk reduction of HAV in Shanghai.
- Impact of childhood HA vaccination cannot be seen soon in well developed area where adults are at higher risk than children. However, the impact will be more and more clear in the near future.

Sero-prevalence of Anti-HAV in 1988 & 1997



Declining HAV risk in Shanghai, 1988 - 1997

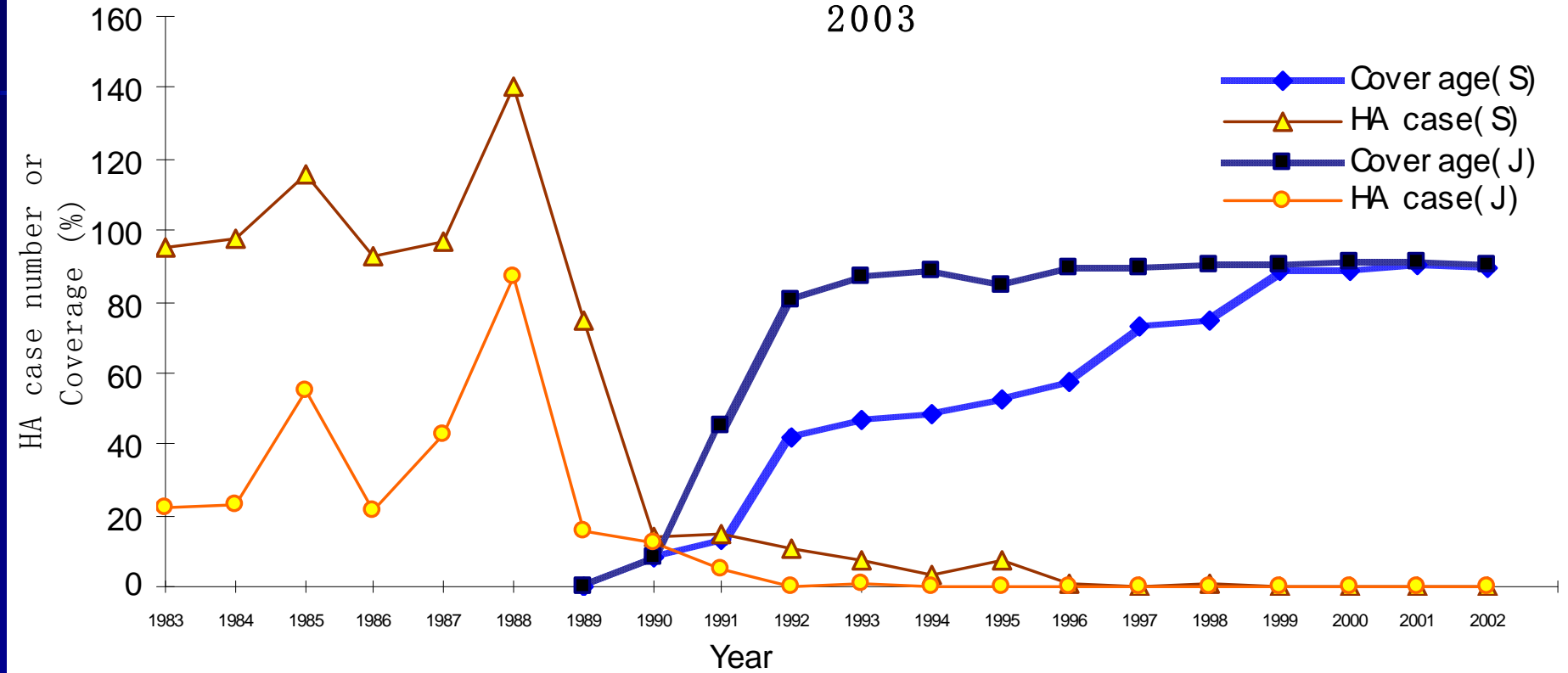
- Sero-prevalence of anti-HAV was much lower in 1997 than in 1988.
- The risk reduction was unrelated to HAV vaccination.
- The higher risk in adults in 1997 was due to a shellfish associated, large HA outbreak in 1988 involving 300,000 HA cases, mostly in adult age.

Is HAV Eradicable?

Elimination of HAV by vaccination

- In a series of cities and counties highly endemic for HAV in the past, high coverage of children with HAV vaccine has led to elimination of HAV, because adults had already been immune by previous infection.
- Investigation of the need for a booster dose in the future would be critical.
- HAV is eradicable.

Correlation between vaccine coverage & incidence of HA in 1-15 yr old- children, J City and S County, 1983 - 2003



Conclusions

- Both HAV vaccination and changing life style contributed to the rapid decline in HAV risk in China.
- In the well developed regions, the booming economy with changing life style played major role in the risk reduction. Vaccination will play more & more important role in this region in the future.
- HA is eradicable & eventual eradication of the disease would rely on vaccination.
- Further study will be done to trace the changing risk of HAV in China